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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/063,570	05/02/2002	Audrey Goddard	P3230R1C001-168	2398

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EXAMINER	
HUNNICUTT, RACHEL KAPUST	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 05/31/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/063,570	GODDARD ET AL.	
	Examiner	Art Unit	
	Rachel K. Hunnicutt	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 May 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *0505*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RESPONSE TO AMENDMENT

Applicant's amendment filed May 2, 2005 is acknowledged. Claim 6 has been canceled. Claim 1 has been amended. Claims 1-5 are pending and under consideration. The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action.

Claim Rejections/Objections Withdrawn

The objection to the specification regarding the use of trademarks is withdrawn in response to Applicants' amendment to the specification.

The objection to the specification for containing an embedded hyperlink is withdrawn in response to Applicants' amendment to the specification.

The rejection of claims 1 and 4 under 35 U.S.C. 101 as being directed to non-statutory subject matter is withdrawn in response to Applicants' amendment to the claims. The rejection of claim 6 under 35 U.S.C. 101 as being directed to non-statutory subject matter is withdrawn in response to Applicants' cancellation of the claim.

The rejection of claim 6 under 35 U.S.C. 101 as not be supported by either a specific and substantial asserted utility or a well-established utility is withdrawn in response to Applicants' cancellation of the claim.

The rejection of claims 1-5 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is withdrawn in response to Applicants' amendment to the claims. The rejection of claim 6 under 35 U.S.C. 112, second paragraph, is withdrawn in response to Applicants' cancellation of the claim.

The rejection of claim 6 under 35 U.S.C. 112, first paragraph, as not being enabled because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility, is withdrawn in response to Applicants' cancellation of the claim.

Rejections Maintained

Claim Rejections - 35 USC § 101

The rejection of claims 1-5 under 35 U.S.C. 101 is maintained for reasons of record on p. 3-4 of the office action of paper no. 0105.

Applicants argue that mRNA for the PRO3566 polypeptide is more highly expressed in normal skin compared to melanoma tumor, and in esophageal tumor compared to normal esophagus (p. 13 of the response). Applicants further argue that a change in the level of mRNA for a particular protein generally leads to a corresponding change in the level of the encoded protein. Applicants refer to a declaration of J. Christopher Grimaldi (Exhibit 1) and argue that "the biological significance of the data, or the role of PRO3566 in cancer, is not necessary to use the claimed polypeptides as cancer diagnostic tools" (p. 15 of the response). Applicants argue that Exhibit 1 teaches that the DNA libraries used in the gene expression studies were made from pooled samples of normal and of tumor tissues. Grimaldi states in section 6 that "I conducted a semi-quantitative analysis of the expression of the DNA sequences of interest in normal versus tumor tissues. Expression levels were graded according to a scale of +, -, and +/- to indicate the amount of the specific signal detected. Using the widely accepted technique of PCR, it was determined whether the polynucleotides tested were more highly expressed, less expressed, or whether expression remained the same in tumor tissue as compared to its normal counterpart. Because this technique relies on the visual detection of ethidium bromide staining of PCR products on agarose gels, it is reasonable to assume that any detectable differences seen between two samples will represent at least a two fold difference in cDNA."

Furthermore, in another declaration of J. Christopher Grimaldi (Exhibit 4), Grimaldi states that when a gene is overexpressed, the gene product or polypeptide will also be overexpressed (p. 18 of response). The declaration of Dr. Paul Polakis avers that mRNA levels typically correlate with an increase in abundance of the encoded protein (p. 18 of response).

Applicants further cite Orntoft *et al.*, Hyman *et al.*, and Pollack *et al.* in support of the argument that in the vast majority of cases, the combined teachings of the art teach that gene amplification influences gene expression and that gene expression influences protein levels. In addition, Applicants refer to the declaration of Dr. Ashkenazi and cited references Hanna and Mornin who teach that even if higher levels of mRNA do not correlate with an increase in abundance of the encoded protein, that type of information is also useful in diagnosing and treating patients.

Applicants' arguments have been fully considered but have not been found to be persuasive. A utility of being a diagnostic target for melanoma or esophageal tumors is a utility that requires or constitutes carrying out further research to identify or reasonably confirm a "real world" context of use. This is not a substantial utility. In Example 30, Applicants teach that PRO3566 was overexpressed in normal skin and esophageal tumor than in melanoma tumor and normal esophagus tissue. There is no guidance in the specification as to how high the levels of overexpression are. There is no information in the specification as to the differences in expression or whether the results were statistically significant. Applicants have provided no indication of the nature or number of samples that were used. The declaration of Grimaldi does not teach the level of reproducibility or the level of reliability of the results. If a clinician took a skin or esophageal tissue sample from a patient with suspected melanoma or esophageal cancer, what is the likelihood that when compared with normal tissue, the level of PRO3566 from the patient would be higher or lower? How many samples would be needed? What sensitivity would be needed? Applicants have provided no indication of the nature or number of samples that were used.

The only thing Applicants teach is that the gene was "more highly expressed", and this does not enable the skilled artisan to differentiate amongst expression levels in order to diagnose any diseases. On p. 19 of the response, Applicants state that when a gene is overexpressed, the corresponding protein will generally also be overexpressed. However, Chen *et al.* teach that correlation between protein levels and mRNA expression can vary depending upon the protein (Chen *et al.* (2002), *Mol. Cell. Proteomics* 1.4: 304-313). Of 165 protein spots studied by Chen *et al.*, only 17% of the samples showed a statistically significant correlation between mRNA and protein (p. 311). Some of the proteins actually demonstrated a negative correlation with the mRNA expression values (p. 311). One skilled in the art would need to do further research to

determine whether or not the PRO 3566 polypeptide levels increased or decreased significantly in the tumor samples. Such further research requirements make it clear that the asserted utility is not yet in currently available for, *i.e.* it is not substantial. Without more specifics about necessary sample size, expression level range for normal and tumor tissues, types of skin and esophageal tissue that can be used, and other questions, the specification has not provided the invention in a form readily usable by the skilled artisan such that significant further experimentation is unnecessary.

Claim Rejections - 35 USC § 112

The rejection of claims 1-5 under 35 U.S.C. 112, first paragraph for lack of enablement because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility, is maintained for reasons of record on p. 4 of paper no. 0105.

Conclusion

NO CLAIMS ARE ALLOWED.

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rachel K. Hunnicutt whose telephone number is (571) 272-0886. The examiner can normally be reached on Mon-Fri 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

RKH
5/24/05

JANET ANDRES
PRIMARY EXAMINER